ORGANIC-INORGANIC COMPOUND POROUS BODY AND MANUFACTURING METHOD THEREOF

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Abstract of **JP 2003159321 (A)**

PROBLEM TO BE SOLVED: To provide the organic-inorganic compound multiple porous bodies that make it possible to facilitate an immersion of a humor or the like, boncing with the bones of a living body and reconstruction of biological osteous tissues in an early stage and are practically used as a footing of tissue reconstructions, prosthetic material, bone filler, intervening substance between an implant and biological osteous tissues, substitute for cancellous bone, a carrier for sustained release of drugs or the like as well as the manufacturing method thereof. ; SOLUTION: The organic-inorganic compound multiple porous bodies are composed of a structure in which inorganic particles such as the particles of biologically active bioceramics or the like are substantially and uniformly dispersed in organic polymers such as in vivo resolving absorptive polymers and have consecutive stomata of roughly 100-400 [mu]m in inner diameter and the content of inorganic particles as much as 60-90 weight%, leaving partially exposed inorganic particles on the surface and the inner surface of stomata. This multiple porous body can be obtained by manufacturing a fiber aggregate from a suspension of inorganic particles dissolved in a volatile solvent and dispersed thereon, which was heated and pressurized to be formed into a multiple porous fiber aggregate and immersed in a volatile solvent before the solvent was removed. ; COPYRIGHT: (C)2003,JPO

* NOTICES *

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2.**** shows the word which can not be translated.
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CLAIMS

[Claim(s)]
[Claim 1]Organic - inorganic matter compound porous body which an inorganic powder grain distributed uniformly substantially in organic polymer, had a continuation stoma inside, and a part of inorganic powder grain has exposed to the surface and a stoma inner surface.
[Claim 2]A nonwoven fabric state fiber aggregate is built with suspension which dissolved organic polymer in a volatile solvent, was made to distribute an inorganic powder grain, and was prepared, It is a porous body produced by removing this solvent after carrying out pressing and immersing a fiber set Plastic solid under heating of this at a porous fiber set Plastic solid, nothing, and a volatile solvent, Organic - inorganic matter compound porous body which an inorganic powder grain distributed uniformly substantially in organic polymer, had a continuation stoma inside, and a part of inorganic powder grain has exposed to the surface and a stoma inner surface.
[Claim 3]The organic - inorganic matter compound porous body according to claim 1 or 2 in which porosity is 50 to 90% and a continuation stoma forms 50 to 90% of the whole stoma.
[Claim 4]The organic - inorganic matter compound porous body according to any one of claims 1 to 3 whose apertures of a continuation stoma are 100-400 micrometers of profiles.
[Claim 5]The organic-inorganic matter compound porous body according to any one of claims 1 to 4 whose content of an inorganic powder grain is 60 to 90 weight %.
[Claim 6]The organic-inorganic matter compound porous body according to any one of claims 1 to 5 which thickness is 1-50 mm and has thick three-dimensional cubic shape.
[Claim 7]a living body to whom organic polymer is a biodegradation absorption polymer and an inorganic powder grain has the mean particle diameter of 10

micrometers or less -- the organic-inorganic matter compound porous body according to any one of claims 1 to 6 which is an activity bioceramics powder.
[Claim 8]organic polymer is biodegradation total absorption nature polymer -- an inorganic powder grain -- a living body of total absorption nature -- the organic-inorganic matter compound porous body according to any one of claims 1 to 6 which is an activity bioceramics powder.
[Claim 9]Biodegradation total absorption nature polymer A block copolymer of Polly D, L-lactic acid, L-lactic acid, and D and L-lactic acid, A copolymer of lactic acid and glycolic acid, lactic acid and a copolymer of p-dioxa non, it is either of the block copolymers of lactic acid and ethylene glycol -- a living body of total absorption nature -- an activity bioceramics powder, Non-temporary quenching, uncalcinated hydroxyapatite, JIKARUSHIUMU phosphate, The organic-inorganic matter compound porous body according to claim 8 which is one powder of tricalcium phosphate, tetracalcium phosphate, octacalcium phosphate, calcite, cera liveliness, a JIOPU site, and natural coral.
[Claim 10]Organic inorganic composite given in Claim 7 whose compressive strength is 1 - 5MPa, Claim 8, or Claim 9.
[Claim 11]Organic inorganic composite given in Claim 7 to which oxidation treatments, such as corona discharge and plasma treatment, were performed, Claim 8, Claim 9, or Claim 10.
[Claim 12]A nonwoven fabric state fiber aggregate is built with suspension which dissolved organic polymer in a volatile solvent, was made to distribute an inorganic powder grain, and was prepared, A manufacturing method of organic - inorganic matter compound porous body removing this solvent after carrying out pressing and immersing a fiber set Plastic solid under heating of this at a porous fiber set Plastic solid, nothing, and a volatile solvent.
[Claim 13]Carry out pressing under heating of a fiber aggregate, face considering it as a porous fiber set Plastic solid, build a preforming thing with a void which hardened a fiber aggregate under heating and application of pressure first, and continued, and it ranks second, The manufacturing method according to claim 12 considering it as a fiber set Plastic solid of porosity with intensity which carried out pressing of the preforming thing, and by which an intercommunicating porosity hole was adjusted more under high voltage.
[Claim 14]The manufacturing method according to claim 12 by which being immersed facing that a porous fiber set Plastic solid is immersed in a volatile solvent, filling up with a fiber set Plastic solid a predetermined mold which has much fine pores, and holding form.
[Claim 15]Claim 7, Claim 8, Claim 9, Claim 10, a living body bone that consists of an organic-inorganic matter compound porous body indicated to either of Claim 11, or a scaffold for cartilaginous tissue reproduction.

[Claim 16]Claim 7, Claim 8, Claim 9, Claim 10, living body prosthetic dentistry material that consists of an organic-inorganic matter compound porous body indicated to either of Claim 11.
[Claim 17]Claim 7, Claim 8, Claim 9, Claim 10, a bone filler that consists of an organic-inorganic matter compound porous body indicated to either of Claim 11.

[Claim 18]Inclusion between implant and a body bone organization which consist of an organic-inorganic matter compound porous body indicated to Claim 7, Claim 8, Claim 9, Claim 10, or Claim 11.
[Claim 19]A substitute of a cancellous bone of bulk form which consists of an organic-inorganic matter compound porous body indicated to Claim 7, Claim 8, Claim 9, Claim 10, or Claim 11.
[Claim 20]Claim 7, Claim 8, Claim 9, Claim 10, a carrier for drug gradual release that consists of an organic-inorganic matter compound porous body indicated to either of Claim 11.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention about organic-inorganic matter compound porous body The scaffold especially for body bone anagenesis (Scaffold), It is related with organic-inorganic matter compound porous body suitable for the use of the inclusion between prosthetic dentistry material, a bone filler, the implant, and a body bone organization, the substitute of a cancellous bone, the carrier for drug gradual release of DDS (Drug Deliverly System), etc.
[0002]
[Description of the Prior Art]As an inorganic porous body aiming at a medical-application way, temporary quenching or the porous ceramics produced by sintering (Calcined, Sintered) are known in Ceramics Sub-Division, for example. However, although these porous ceramics are hard for using it for uses, such as a scaffold for body bone organization reconstruction, and prosthetic dentistry material, since there is a fault that it is weak, it is always apprehensive about breakage by few postoperative shocks. It is also difficult to process it and to change the form of porous ceramics at the operation spot so that the form of the lacking part of a body bone organization may be suited.
[0003]On the other hand, the sponge etc. which were indicated by JP,63-64988,B are known as an organic porous body aiming at a medical-application way, for example. This sponge is sponge which has ordinarily a continuation stoma which is used as a prosthetic dentistry material at the time of the hemostasis at the time of an operation, or a suture of a living body's tissues (for example, organ etc.), and consists of polylactic acid of biodegradation absorptivity. This sponge dissolves polylactic acid in benzene or dioxane, and is manufactured by the method which freeze-dries the polymer solution and to which a solvent is made to sublimate.

[0004]However, the porous body manufactured by a freeze drying method like the above-mentioned sponge is difficult for sublimation to take a long time and to remove a solvent thoroughly, and the thickness is as thin as 1 mm or less (usually about hundreds of micrometers), and it is actually difficult to manufacture a not less than several millimeters thick porous body. Although various methods are examined besides the above-mentioned freeze drying method as other methods of building the porous body which has a continuation stoma, it is difficult for all to obtain a several millimeters thick porous body. Such a thin porous body is geometrically applied to the complicated and comparatively large three dimensional space of for example, a body tissue damaged area, and there is difficulty in considering it as the material which aims at organization reconstruction of a three-dimensional damaged area, demonstrating the function as primary prosthetic dentistry material. Then, thickness is large and what can work on a free-shaped three-dimensional cube before an operation or after the operation is called for.
[0005]The powder of fusibility, such as NaCl etc. of the predetermined size which is water solubility, is mixed so much to polymer as another leading method of building a continuation porous body, After building the molded product of sheet shaped closing in, the melting which forms the continuous pores of the same path as this powder by being immersed in water (solvent) and eluting this powder is known, but since it is difficult to elute this powder thoroughly, it is limited to the continuation porous body of closing in. If the ratio of a water-soluble powder becomes high, it will be hard to become an open cell. And when using this porous body as an embedding material in the living body, there is a problem of troubling to the toxicity of this powder that remains.
[0006]the above-mentioned sponge -- like -- a living body -- the porous body which does not include inorganic powder grains, such as activity bioceramics, Direct unity with body bone organizations, such as a bone and a cartilage (direct bondingability to bone), Since conductivity (osteoconductivity), replaceability (bone replacement), etc. are scarce and the tissue which is not osteoblast invades and intervenes, It finishes as a remarkable long period of time is taken for a living body's osseous tissue to replace thoroughly and to reproduce it or it is not replaced.
[0007]Then, seeding of these people is carried out in osteoblast, and they become a scaffold of a three-dimensional cube, the lacking part of a big bone -- a pons -- it already applied for the porous body with large thickness which has a continuation stoma which becomes an inside which can be planted for me from the biodegradation absorption polymer which the bioceramics powder contained (Tokuganhei8-229280).
[0008]This porous body is based on the manufacturing method of the porous

body called a solution sedimentation method. Namely, dissolve a biodegradation absorption polymer in a mixed solvent with the nonsolvent of a high boiling point from the solvent and its solvent, and. A bioceramics powder is distributed, suspension is prepared, a mixed solvent is aerated at low temperature from the boiling point of a solvent from this suspension, and it is based on the method of settling the biodegradation absorption polymer which includes a bioceramics powder.

[0009]The formation principle of the porous body by this solution sedimentation method is as follows. If a mixed solvent is aerated at low temperature from the boiling point of a solvent from the above-mentioned suspension, the low solvent of the boiling point will exhale preferentially and the ratio of the high nonsolvent of the boiling point will rise gradually, and when a ratio with a solvent and nonsolvent is reached, it becomes impossible that is, for a solvent to dissolve polymer. Therefore, the bioceramics powder which polymer started a deposit and precipitate and has started sedimentation at the beginning is included, It is fixed the polymer which deposited and precipitated contracting and solidifying with the nonsolvent of a high ratio, and containing a bioceramics powder, and the cellular structure in the state where the mixed solvent was included by the connected thin cell wall of polymer is formed. And fine pores are built, while the remaining solvents destroy some cell walls, it disappears and exhalation and the high nonsolvent of the boiling point also exhale gradually through these fine pores, and it exhales and disappears thoroughly finally. As a result, the bioceramics powder content porous body with which the remains of a reservoir of the mixed solvent wrapped in the cell wall of polymer were connected as a continuation stoma is formed.

[0010]

[Problem to be solved by the invention]The above-mentioned solution sedimentation method is the epoch-making method of forming a porous body with large thickness of high expansion ratio from low foaming magnification, and can obtain the three-dimensional porous body of the block like shape which has a thickness of several millimeters thru/or tens of mm. So, in the scaffold of the osteoanagenesis of cubic shape (three-dimensional spacial configuration), it is very useful.

[0011]However, with suspension which contained a bioceramics powder in large quantities, a fault of this method. When a bioceramics powder which belongs to comparatively big particle size distribution among mean particle diameter starts sedimentation at the beginning which begins solvent vaporization and polymer starts a deposit and precipitate, Since a remarkable bioceramics powder has already sedimented with a concentration gradient towards a pars basilaris ossis occipitalis, content of a porous body obtained increases as content of a

bioceramics powder is not selectively uniform and approaches the bottom side from the upper surface side of a porous body. Thus, content cannot use an uneven porous body with a concentration gradient for uses, such as a scaffold for osseous tissue reconstruction, prosthetic dentistry material, or a bone filler, easily effectively. This problem is thoroughly unsolvable although it is possible to improve to some extent by controlling sedimentation velocity of a bioceramics powder, etc. It is difficult especially to consider it as a porous body with homogeneous and equal concentration which contains a thing bioceramics powder 30weight % or more for three-dimensional bone reconstruction.

[0012]A porous body with little content of a bioceramics powder manufactured by an above-mentioned method, Since most bioceramics powders are included by cell wall of polymer and it is hard to expose it to an inner surface of a continuation stoma, When it embeds in the living body, a conduction operation of a body bone organization by a bioceramics powder is hard to be demonstrated from the time of embedding, and there is a problem that living body activity is revealed with a bioceramics powder exposed [decomposition of polymer which forms a skin of a continuation stoma inner surface].

[0013]Though a porous body manufactured by an above-mentioned method chooses a super-thin grain, if it needs to carry out content of a bioceramics powder to to about at most 30 weight % and a large quantity is made to contain it from this, Since a bioceramics powder sediments much more easily, there is a limit that the bottom side of a porous body obtained becomes very weak including a lot of bioceramics powders.

[0014]Although a porous body manufactured by an above-mentioned method usually has a rate (porosity) as large as not less than 80% that a continuation stoma occupies, Generally, since only several micrometers thru/or tens of micrometers, and a comparatively small continuation stoma are obtained, an aperture cannot say that a form of an aperture ideal for invasion and growth of osteoblast inside a porous body and a hole is formed.

[0015]An object of this invention is to provide the manufacturing method to organic-inorganic matter compound porous body which can solve these problems.

[0016]

[Means for solving problem]An inorganic powder grain distributes uniformly substantially in organic polymer, organic - inorganic matter compound porous body concerning this invention is a porous body which has a continuation stoma inside, and a part of inorganic powder grain exposes it to the surface and stoma inner surface. And a continuation stoma is adjusted by about 100-400 micrometers in suitable aperture for osteoblast to increase and invade and be stable, and an inorganic powder grain is contained so much with 60 to 90 weight

%. Thickness of a porous body is as large as 1-50 mm, and has three-dimensional cubic shape.

[0017]Such an organic-inorganic matter compound porous body builds a nonwoven fabric state fiber aggregate with the manufacturing method of this invention, i.e., the suspension which dissolved organic polymer in the volatile solvent, were made to distribute an inorganic powder grain, and was prepared, It can manufacture by the method of carrying out pressing under heating of this, and removing this solvent after ranking second and immersing a fiber set Plastic solid in a volatile solvent, a porous fiber set Plastic solid, nothing, and. As a means which builds a nonwoven fabric state fiber aggregate with suspension, When the means which carries out a spray is adopted preferably and a fiber set Plastic solid is immersed in a volatile solvent, fibrosing suspension, what external force which holds the form of a fiber set Plastic solid is applied for is desirable, and, thereby, a porous body with a mechanical strength is obtained.

[0018]As mentioned above, if the means which carries out a spray is adopted fibrosing the adjusted suspension as a means which builds a fiber aggregate, Fiber of organic polymer included the inorganic powder grain becomes entangled mutually, and ****s at a mutual point of contact, fiber carries out set solidification by the vaporization of a volatile solvent, and a nonwoven fabric state fiber aggregate with arbitrary heavy-gage form is formed. This fiber aggregate has the continuous space whose interval between fiber which carried out welding solidification is about hundreds of micrometers although fiber interspace spare time is not a cell-like hole (round cell space), and an inorganic powder grain is included by fiber, covers the whole fiber aggregate, and is distributed uniformly. Pressing is carried out under heating of this fiber aggregate, a porous fiber set Plastic solid is built, and if immersed in a volatile solvent, holding that form applying external force, fiber will contract and unite. And a fibrous form disappears substantially and fiber interspace spare time becomes the porosity matrix which carried out the shape change to the continuation stoma object with the cellular structure which has a radius of circle. And that part exposes to a stoma inner surface the inorganic powder grain contained so much with this transformation, and. It exposes by ********** to such an extent that an inorganic powder grain does not drop out easily on the surface, and organic-inorganic matter compound porous body made into the purpose, i.e., an inorganic powder grain, distributes uniformly substantially with high content, and organic - inorganic matter compound porous body which the part exposed to the surface or the inner surface of a continuation stoma is obtained. Of course, when a skin is formed in the surface of conditions, an inorganic powder grain may be exposed by carrying out sanding. This compound porous body by adjusting the external pressure for

holding that form, when a fiber set Plastic solid is immersed in a volatile solvent, The average pore size of a continuation stoma is controllable to convenient about 100-400 micrometers for invasion and stabilization of osteoblast, and it is desirable to make porosity into a stoma form with about 50 to 90% of desirable conditions.

[0019]It is possible to make the stoma inside of the body contain uniformly 60 to 90weight % (equivalent to 41-81 volume %, when mean particle diameter is 3 micrometers) of an inorganic powder grain in a manufacturing method of this invention within limits which can fibrose. Since this fiber ****s before an inorganic powder grain sediments, even if it makes it contain so much, rather than a porous body obtained with a solution sedimentation method mentioned above, an inorganic powder grain is distributing uniformly and content can obtain a far high compound porous body eventually. However, if it is high content too much, it will become difficult for the amount of polymer as a binder to decrease, and for a porous body to become weak, and to maintain form.

[0020]Even if the solvent characteristic has balanced this manufacturing method, is already used as organic polymer, safety is confirmed, this organic-inorganic matter compound porous body aiming at medical-application ways, such as a scaffold for body bone anagenesis, has comparatively quick decomposition and it becomes a porous body, polymer which is not weak is chosen. Namely, a block copolymer of Polly D in whom it was amorphous or a crystal and non-** were intermingled, L-lactic acid, L-lactic acid, and D and L lactic acid, Biodegradation absorption polymers, such as copolymers of lactic acid, a copolymer of glycolic acid and lactic acid, a copolymer of p-dioxa non and lactic acid, a copolymer of a caprolactone and lactic acid, and ethylene glycol or these mixtures, are used. In consideration of a period of that the viscosity average molecular weight tends to form a nonwoven fabric state fiber aggregate and decomposition absorption in the living body, a thing of 50,000-1 million is used preferably.

[0021]A block copolymer of Polly D who originates in a monomer ratio and shows amorphism nature especially, L-lactic acid, L-lactic acid, and D and L lactic acid, Biodegradation total absorption nature polymer, such as a copolymer of lactic acid and glycolic acid, lactic acid, a copolymer of p-dioxa non, If it is suitable and these polymer is used under heating of this, in view of the solvent characteristic when processing a fiber set Plastic solid which carried out pressing by a volatile solvent when forming a nonwoven fabric state fiber aggregate and, Even if it includes a lot of inorganic powder grains, it has about the same compressive strength (compressive strength of about 1-5 MPa) as a cancellous bone easily, Organic - inorganic matter compound porous body by which can carry out heat modification at low temperature (about 70 **)

comparatively unlike a porous body of a ceramic simple substance, hydrolyzes promptly in the living body, and total absorption is carried out in six to 12 months can be obtained. A compound porous body which has such the characteristic is very preferred as a biomechanical material with which a lacking part of a body bone is filled up. Although it is a complex therefore, it has also left an advantage peculiar to thermoplastic polymer which can prepare a form so that heat modification may be carried out during an operation unlike material of only Ceramics Sub-Division and it may agree in a lacking part.

[0022]Since it hydrolyzes and a molecular weight of biodegradation total absorption nature polymer affects time until total absorption is carried out, and propriety of fibrosis, polymer which has the viscosity average molecular weight of 50,000-1 million as mentioned above is used. Although time when polymer which has viscosity average molecular weight smaller than 50,000 is hydrolyzed by a low molecule of oligomer thru/or a monomeric unit is short, it is difficult to carry out a spray and to form a bicomponent fiber aggregate, fibrosing, since stringiness runs short. Since it takes a long period of time to carry out complete hydrolysis of it, polymer which has larger viscosity average molecular weight than 1 million is unsuitable as polymer of a compound porous body, when aiming at early substitution with a body tissue. Although it changes with polymer, that desirable viscosity average molecular weight is the profiles 100,000-300,000, and if polymer which has a molecular weight of this range is used, it can obtain a compound porous body of this invention which formation of a fiber aggregate becomes easy and has moderate hydrolysis completion time.

[0023]In organic-inorganic matter compound porous body aiming at the above-mentioned medical-application way, as an inorganic powder grain, there is living body activity and a bioceramics powder which has good osseous conduction capacity (it is supposed that bone induction potency is sometimes shown) and good biocompatibility is used. As such a bioceramics powder, for example, a surface living body -- activity calcination, temporary calcination hydroxyapatite, and apatite WORASUTO night crystallized glass. Non-temporary quenching of living body activity and total absorption nature in the living body, uncalcinated hydroxyapatite, Powders, such as JIKARUSHIUMU phosphate, tricalcium phosphate, tetracalcium phosphate, octacalcium phosphate, calcite, cera liveliness, a JIOPU site, and natural coral, are mentioned. A thing which made an alkaline inorganic compound, a basic organic matter, etc. adhere to the surface of these powders is also usable. According to a Reason it is ideal that succeed in total replacement arthroplasty with one's body tissue, and anagenesis is performed. A bioceramics granular material of total absorption nature in the living body which total absorption is carried out and is thoroughly replaced by an osseous tissue also in these in the living body is preferred, Activity is the

largest, they are excellent in osseous conduction capacity, are excellent in biocompatibility, their harmfulness is low, and since especially non-temporary quenching, uncalcinated hydroxyapatite, tricalcium phosphate, and octacalcium phosphate are absorbed by living body for a short period of time, they are the optimal.

[0024]If it is preferred that particle diameter uses a thing of 10 micrometers or less as for the above-mentioned bioceramics powder and a bioceramics powder of larger particle diameter than this is used, When carrying out a spray, fibrosing suspension which mixed this powder, fiber is cut short, and even if it becomes difficult to form a fiber aggregate and it is able to form a fiber aggregate, there will be a possibility of a bioceramics powder sedimenting somewhat by the time fiber solidifies, and distributing unevenly. Since full absorption takes a long time and a tissue reaction in the meantime is sometimes revealed even if it is total absorption nature, a thing of a size over 20-30 micrometers is not preferred.

[0025]If still more desirable particle diameter of a bioceramics powder is 0.2-5 micrometers and such a bioceramics powder is used, Even when fibrosing thinly suspension which mixed this powder to high concentration with about 1-3 micrometers and forming a fiber aggregate in it like this invention, Fiber is hard to be cut, and when it is high concentration like this invention, after this powder comes to be included by fiber in the state where it exposed from fiber and carries out dipping treatment of the fiber aggregate by a volatile solvent, this powder serves as a compound porous body exposed from the surface or an inner surface of a continuation stoma.

[0026]A carrier or a bone filler for a scaffold [in / in content of a bioceramics powder / tissue engineering], or DDS, In the case of organic-inorganic matter compound porous body aiming at medical-application ways, such as a substitute of an anomaly-like cancellous bone (Allograft: piece of congener different **), it is preferred to consider it as 60 to 90 weight %, considering the living body activity effect of bioceramics. When an aggregate of fiber which included an inorganic powder grain like this invention is formed, a fiber set Plastic solid which carried out pressing of this under heating is immersed in a volatile solvent and it obtains a compound porous body, Since a lot of inorganic powder grains can be made to contain within limits which can fibrose, content of a bioceramics powder can be raised as mentioned above with 60 to 90 weight % (a volume ratio at the time of mean particle diameter of 3 micrometers is equivalent to a high ratio of 41 to 81%). Since it will go out short and will not become satisfactory fiber, when fibrosing if content of a bioceramics powder exceeds 90 weight %, if formation of a fiber aggregate becomes difficult and is less than 60 weight % on the other hand, Bioceramics powders run short, and since what is exposed to the surface is little, living body activity which originates in a

bioceramics granular material from the first stage embedded to a living body is hard to be revealed.

[0027]Although porous ceramics produced by sintering Ceramics Sub-Division, such as hydroxyapatite, are hard, since it is weak, since thin material breaks easily with external force or is missing, it is dissatisfied as implant. On the other hand, a compound porous body which made a biodegradation absorption polymer which is amorphism nature especially contain a bioceramics granular material, Even when content of a bioceramics granular material is as high as 60 to 90 weight %, by the joint (binding) effect of the polymer. Compressive strength of the cancellous bone average holding flexibility which is not weak, and since it specifically has about [1MPa-5MPa] compressive strength, it is suitably used as substitution (for of-the-same-kind bone grafting: substitution of Allograft bone) of a cancellous bone, a bone filler, prosthetic dentistry material and a scaffold for reproduction, or a carrier of DDS.

[0028]moreover -- as another leading use -- a body bone (a bone, a cartilage) -- inclusion between artificial implant of business is mentioned. For example, since it is inescapable that a crevice arises among living bodies when embedding an artifact which has the high concentration built with polylactic acid system polymer of entering [which is the osteosynthesis material of living body activity and living body absorptivity] bioceramics powder, If it intervenes and this compound porous body is directly contacted to an osseous tissue in the meantime, osteoconductivity will be revealed notably. Although this works effectively by various parts of a body bone, bone derivation (concomitant use with cytokine) and bone conduction can be brought about into a hollow-ized intense bone of osteoporosis (osteoporosis) by embedding a sternum lock-pin which made a Ko Honda object penetrate in the case of median sternotomy for example to the Masanaka bone. Or it can use as an underlay of this kind of plate, and adhesion with a bone can also be aimed at. A use as inclusion of a living body and an artifact has aiming at [much] direct combination to an artificial intervertebral disk and a centrum end plate (endplate) etc.

[0029]Although porosity (total porosity) is not less than 50% and this organic - inorganic matter compound porous body is technically possible to about 90%, If both sides of physical intensity of this compound porous body, invasion of osteoblast, and stabilization are taken into consideration, 60 to 80% of a profile is good, and considering efficiency of invasion of osteoblast to the central part of a compound porous body, a thing of the whole stoma for which a continuation stoma occupies 70 to 90% above all 50 to 90% is preferred.

[0030]As for a continuation stoma of this organic-inorganic matter compound porous body, that aperture is adjusted to 100-400 micrometers of profiles. It turns out that an effect fades as it has already succeeded in an aperture of

porous ceramics, invasion of osteoblast, and research of stabilization many times, and 300-400 micrometers in their aperture is the most effective for mineralization and separates them from it, considering the result. So, although an aperture of a compound porous body of this invention is adjusted by 100-400 micrometers of profiles as mentioned above, a center of a distribution may be 200-400 micrometers including a thing of an aperture of the range of 50-500 micrometers.

[0031]Incidentally, when porosity (total porosity) is higher than 90%, since intensity of a compound porous body falls, a possibility of destroying easily during [in the living body] embedding is large [an aperture of a continuation stoma is larger than 400 micrometers, and]. On the other hand, when an aperture is smaller than 100 micrometers and porosity is lower than 50%, intensity of a compound porous body improves, but invasion of osteoblast is difficult, it hydrolyzes and time until it carries out full absorption becomes long. However, a small compound porous body of low porosity of such an aperture is available by a case as a material which desires to maintain sustained-release [of comparatively long time to do simultaneously with decomposition of polymer as a carrier of DDS]. A more desirable aperture of a continuation stoma is 150-350 micrometers, and more desirable porosity (total porosity) is 70 to 80%. A ratio of a continuation stoma to an aperture of a continuation stoma, and the whole stoma, As mentioned above, it is controllable by regulation of a compression ratio when carrying out pressing of the fiber aggregate and making with a fiber set Plastic solid, and regulation of the external pressure for form maintenance in case the form is held and a fiber set Plastic solid is immersed in a volatile solvent.

[0032]The above organic - inorganic matter compound porous bodies can be used, for example as implant of various form, being able to embed to a deficit part of a body bone. Since it can embed that there is no crevice in defective parts by making it change so that a compound porous body may be heated at about 70 ** using the thermoplasticity of organic polymer and it may agree in form of defective parts in that case, it becomes possible to do embedding work simply and correctly. A scalpel can also use from arbitrary form during an operation for hardness of toughness which organic polymer has, and a ceramic powder, cutting without form collapse.

[0033]A compound porous body For example, since body fluid will permeate an inside of a compound porous body promptly through inside of a continuation stoma from the surface of a compound porous body if it embeds in a living body's osseous tissue as mentioned above, Since hydrolysis of a biodegradation absorption polymer advances almost simultaneous from both sides the surface of a compound porous body, and inside a continuation stoma, The whole porous

body is covered and decomposition advances uniformly (however, it gets wet, and a bioceramics powder with living body liquid which contained the characteristic so much and was exposed to the surface gets wet, and with the characteristic.). It is improving more remarkably than a case of only polymer, or polymer gets wet, and oxidation treatments, such as corona discharge, plasma treatment, and hydrogen-peroxide-solution processing, may be performed to a porous body in order to make more effective invasion of a cell which should also improve the characteristic and should be increased, and growth. And a compound porous body embedded to a part which osteocyte exists or contacts osteocyte, With osseous conduction capacity of a bioceramics powder exposed to the surface, conduction formation is carried out promptly, and an osseous tissue becomes the bony trabecula (trabecularbone) and grows up to be a layer part of a compound porous body, Since a compound porous body combines with a deficit part of a body bone within a short period of time, and an osseous tissue invades also into an inside of a compound porous body, osteoblast conducts and it grows up with osseous conduction capacity of a bioceramics powder exposed to a stoma inner surface, it couples directly with a circumference bone. This phenomenon becomes remarkable with advance of decomposition of a biodegradation absorption polymer, and is gradually replaced by a circumference bone. And decomposition absorption of the polymer is carried out thoroughly eventually, and when a bioceramics powder is absorptivity in the living body, a bioceramics powder is also absorbed thoroughly, and it is thoroughly replaced by grown-up osseous tissue, and reproduction of a bone lacking part is completed.

[0034]Speed by which decomposition absorption is carried out as a scaffold for living body reconstruction of which the above total replacement arthroplasties are required is balanced, By making various growth factors, such as cytokine which are beforehand filled up in a stoma, or were dissolved beforehand and made to support in polymer, drugs for various therapies, an antimicrobial agent, etc. release gradually, living body reproduction and sick recovery can be promoted, or it can be made effective. It is clear that the above-mentioned compound porous body naturally becomes a filler and prosthetic dentistry material of a deficit organization with combination with a bone (Allograft bone) independent or of the same kind as point ** was carried out.

[0035]Although the above-mentioned organic - inorganic matter compound porous body is total replacement arthroplasty or the things in part aiming at a medical-application way, such as inclusion between a scaffold for replaced type body tissue reproduction, a carrier of drugs, prosthetic dentistry material, a bone filler, implant, and a body tissue, and a substitute of a cancellous bone, In the case of organic-inorganic matter compound porous body aiming at other

uses, according to a use, selection use of polymethylmethacrylate, polyvinyl acetate, polyvinyl chloride, polyurethane, polyalkylene oxide, and various kinds of general-purpose resin meltable to other volatile solvents is suitably carried out as organic polymer. And as for an inorganic powder grain, according to a use, selection use of various kinds of industrial use fillers, a functional filler, a ceramic powder, carbon powder, the carbon nanotube, etc. is carried out suitably.

[0036]Next, a manufacturing method of this invention is explained.

[0037]According to the manufacturing method of this invention, first, the above-mentioned organic polymer is dissolved in a volatile solvent, and the above-mentioned inorganic powder grain is distributed uniformly, and suspension is prepared. Solvents, such as low-boiling-point dichloromethane which vaporizes easily at a temperature a little higher than ordinary temperature as a volatile solvent, a dichloroethane, a methylene chloride, and chloroform, are used. To these solvents, nonsolvent in which the boiling point is higher than these solvents. for example, either of alcohol, such as methanol in a range whose boiling point is 60-110 **, ethanol, 1-propanol, 2-propanol, 2-butanol, ter-butanol, and a ter-pentanol, -- a volatile mixed solvent which was independent or mixed two or more sorts is also used.

[0038]Subsequently, suspension is attached to a spray machine to close, and a spray is carried out, fibrosing suspension from a nozzle of a spray machine to an injection body by high-pressure-jet gas [inertness / nitrogen gas]. Thus, if a spray is carried out, it will solidify, while suspension fibroses, it becomes entangled mutually and fiber ****s at a mutual point of contact, a volatile solvent vaporizing, and a nonwoven fabric state fiber aggregate will be formed. What is necessary is to wait for a solvent to vaporize and dry, to repeat again operation which carries out a spray and is made heavy-gage on it, and just to make it become thick [predetermined], after forming this fiber aggregate with a spray, in order to obtain a 5-50 sometimes required as a biomechanical material of a medical-application way mm heavy-gage compound porous body.

[0039]Gauze and the board which consist of other good polyethylene and olefin system resin of detachability, a fluoro-resin, silicon system resin, etc. as an injection body are used. Since a volatile solvent will vaporize through meshes of a net after suspension's fibrosing with a spray and hitting gauze if the injection body in which aeration like gauze is free is used especially, Fiber of the surface by the side of gauze unites, a skin is not produced, and there is an advantage which can form the fiber aggregate which the impregnation of a solvent tends to carry out. The gauze in which the thing of 50-300 meshes is preferred, and has larger meshes of a net than 50 meshes as gauze, Since a volatile solvent does not vaporize easily smoothly, fiber by the side of gauze unites the gauze which

exfoliating from gauze comes to be hard of the formed fiber aggregate, and has meshes of a net smaller than 300 meshes since fiber turns to the back side through meshes of a net, and a skin becomes is easy to be formed. An injection body may use flat gauze or not only a board but convex-curved, and/or three-dimensional gauze and board which carried out the concave bend. When such a three-dimensional injection body is used, there is an advantage which can form the heavy-gage fiber aggregate as the three-dimensional form.

[0040]The fiber aggregate formed by carrying out a spray while fibrosing suspension as mentioned above has a size of fiber interspace spare time as large as hundreds of micrometers, and the percentage (voidage) that fiber interspace spare time occupies is about 60 to 90%. And without an inorganic powder grain's being included by fiber and sedimenting, the whole fiber aggregate is covered and it is distributing uniformly.

[0041]As for the fiber length of this fiber aggregate, it is preferred that it is about 3-100 mm, and, as for a fiber diameter, it is preferred that it is about 0.5-50 micrometers. Fiber unites easily the fiber aggregate which has fiber length of this level and fiber diameter by the impregnation of a next solvent, and it turns into a compound porous body in which fiber disappeared substantially.

[0042]Fiber length is in the tendency which becomes long, so that a molecular weight becomes large mainly depending on the molecular weight of organic polymer, the polymer concentration of suspension, content, particle diameter of an inorganic powder grain, etc., polymer concentration becomes high, the content of an inorganic powder grain decreases and the particle diameter of an inorganic powder grain becomes small. On the other hand, a fiber diameter is in the tendency which becomes thick, so that polymer concentration becomes high mainly depending on the polymer concentration of suspension, the content of an inorganic powder grain, the size of the nozzle of a spray machine, etc., the content of an inorganic powder grain increases and a nozzle becomes large. A fiber diameter changes also with the pressures of injection gas. Therefore, it is required to prepare the content of the molecular weight of polymer, polymer concentration, and an inorganic powder grain, particle diameter and the size of a nozzle, gas pressure, etc. so that it may become the above-mentioned fiber length and a fiber diameter.

[0043]The above-mentioned fiber aggregate ranks second, and under heating, pressing of it is carried out and it is used as a porous fiber set Plastic solid. It is desirable to build the preforming thing which has the void which hardened the fiber aggregate under heating and application of pressure first, and continued in that case, to carry out pressing of the preforming thing under high voltage further more, and to consider it as the fiber set Plastic solid of porosity with the intensity to which the intercommunicating porosity hole was adjusted. Thus,

if pressing is carried out and a porous fiber set Plastic solid is built, the aperture and porosity of a continuation stoma of a compound porous body which are obtained eventually can be adjusted, and the intensity of a compound porous body can also be raised. The grade which a fiber aggregate softens for a while is enough as heating at the time of pressing, and what is necessary is just to perform application of pressure by a pressure compressible so that the aperture of a continuation stoma serves as 100-400 micrometers of profiles so that the porosity of the compound porous body obtained eventually may be 50 to 90%.

[0044]Subsequently, after immersing this fiber set Plastic solid in a volatile solvent and making this solvent permeate an inside of a Plastic solid, this solvent made to permeate is removed. When a fiber set Plastic solid is immersed in a volatile solvent, it is preferred to be immersed holding form, where it filled up with a fiber set Plastic solid a predetermined mold which has much fine pores and a pressure is applied to a fiber set Plastic solid from the outside. A solvent is poured on the upper surface of a fiber set Plastic solid, and it may be made to make it permeate. As a method of removing a solvent, a method of carrying out vacuum suction of the solvent inside a fiber set Plastic solid, etc. are adopted.

[0045]Dichloromethane, a dichloroethane, a methylene chloride which were mentioned above as a volatile solvent, either of alcohol, such as methanol of the above-mentioned [solvents / solvents, such as chloroform and / these], ethanol, 1-propanol, 2-propanol, 2-butanol, ter-butanol, and a ter-pentanol, -- what was independent or mixed two or more sorts is used preferably.

[0046]Since fiber will melt into a solvent from the surface if a fiber set Plastic solid is immersed in a volatile solvent as mentioned above and a solvent is made to permeate an inside of a Plastic solid, Fiber unites, fiber disappears substantially, and a cellular wall is formed where a continuation stoma in which fiber interspace spare time had a radius of circle which has an aperture which is about 100-400 micrometers is left. And it exposes to a stoma inner surface (cellular wall surface), without sedimenting with fusion of fiber, and a part of inorganic powder grain included in fiber is exposed also to the porous body surface. However, what is necessary is to remove by carrying out sanding of this, and just to take measures to which an inorganic powder grain which exists in a surface is exposed, when a skin is formed in the surface. By the above, an aperture has 100-400 micrometers and a large continuation stoma, and a lot of inorganic powder grains distribute uniformly, and organic - inorganic matter compound porous body which an inorganic powder grain exposed to the surface and a stoma inner surface and which is made into the purpose is obtained. In that case, if dipping treatment to a volatile solvent of a fiber set Plastic solid is

performed under 50-60 ** heating, only by neglecting a fiber set Plastic solid for 5 to 10 minutes, fiber can fully unite and a compound porous body made into the purpose can be obtained efficiently.

[0047]Organic-inorganic matter compound porous body obtained by the above manufacturing method, As mentioned already, the scaffold for body bone organization reconstruction, prosthetic dentistry material, a bone filler, The inclusion between the implant and a body bone organization, the substitute of a bulk-shaped cancellous bone, It is effectively used as a carrier for drug gradual release, etc., and follows, Each of inclusion between the scaffold for body bone organization reconstruction, the prosthetic dentistry material, the bone filler, implant, and body bone organization which consist of this organic - inorganic matter compound porous body, substitutes of a bulk-shaped cancellous bone, and carriers for drug gradual release is contained in this invention.

[0048]

[Mode for carrying out the invention]Next, the concrete embodiment of this invention is described.

[0049][Embodiment 1] The polymer solution (100 ml of concentration-DLLA4g / dichloromethane) in which viscosity average molecular weight dissolved Polly D of 200,000, and L-lactic acid (PDLLA) (mole ratios 50/50 of D-lactic acid and L-lactic acid) in dichloromethane, By homogenizing uniformly the mixture liquid which mixed with ethanol the hydroxyapatite powder (u-HA) which is not calcinated [with a mean particle diameter of 3 micrometers], the suspension which mixed u-HA so that 230 weight sections might become comparatively to PDLLA100 weight section was prepared.

[0050]Use a HP-E airbrush (made by Anest Iwata) as a spray machine, attach the above-mentioned suspension to this to close, and with nitrogen gas of 1.6 kg/cm^2. The spray was carried out to gauze made from polyethylene (150 meshes) left about 120 cm, a fiber aggregate was formed, and a fiber aggregate was exfoliated from gauze. A fiber diameter of this fiber aggregate was about 1.0 micrometer, and, as for fiber length, about 10-20 mm and apparent relative density were 0.2.

[0051]A disc-like fiber set Plastic solid (30 mm in diameter and 5 mm in thickness) was acquired by cutting this fiber aggregate in a suitable size, filling up a cylinder female die 30 mm in diameter, and 30 mm in depth, and compressing with a male so that apparent relative density of a fiber aggregate is set to 0.5.

[0052]Subsequently, after immersing the above-mentioned fiber set Plastic solid in a solvent which consists of dichloromethane which mixed ethanol, making this solvent permeate an inside of a Plastic solid and neglecting it at 60 ** for 10 minutes, vacuum suction removes a solvent inside a Plastic solid,

Organic-inorganic matter compound porous body of 30 mm in diameter, 5 mm in thickness, and 70 weight % of content of u-HA was obtained.

[0053]When a partial cutting side of this compound porous body was observed with an electron microscope, fiber united and disappeared, a continuation stoma which has about 100-400 micrometers in a large aperture was formed, u-HA distributed uniformly, and u-HA was exposed to a stoma inner surface and the surface. A rate (continuation porosity) which occupies apparent relative density of this compound porous body to the whole stoma of 0.5 and a continuation stoma was 75%, and compressive strength was 1.1MPa.

[0054][Embodiment 2] After building a disc-like fiber set Plastic solid (30 mm in diameter, and 5 mm in thickness) as a preforming thing and heating this at 80 ** in gear oven like Embodiment 1, it put into a chamber which has a diameter reduction part from which a size of a diameter differs, and pressed fit in a cylinder whose lower diameter is 10.6 mm. Thus, compressive strength of a fiber set Plastic solid of the shape of a pillar rod by which pressing was carried out under heating was about 2.5 MPa(s).

[0055]Subsequently, pressing to such an extent that a syringe of an equal diameter which a hole opened around is filled up with a fiber set Plastic solid of the shape of this pillar rod, a pressure is applied from that upper surface and undersurface and height of a pillar rod-like fiber set Plastic solid does not change. After being immersed in a solvent (60 **) which consists of dichloromethane which mixed 15weight % of methanol for 10 minutes, this solvent was removed and a compound porous body was obtained.

[0056]An electron microscope photograph of the surface which carried out sanding to a partial cutting side of this compound porous body takes a form of porosity in which fiber disappeared, an aperture comprises an about 150-300-micrometer mixing hole, and a u-HA grain was exposed from the porous body surface or a stoma inner surface. Apparent relative density of this compound porous body was about 0.55, continuation porosity rose to 70% and compressive strength was rising to about 3.5 MPa(s). It is thought that full absorption of this compound porous body is carried out in about six months although it is dependent on an embedding part or size, considering viscosity average molecular weight of PDLLA, a ratio of quantity to occupy, and a biodegradation absorption feature in in vivo of u-HA with a mean particle diameter of 3 micrometers.

[0057][Embodiment 3] Viscosity average molecular weight compounded PDLLA (mole ratios 30/70 of D-lactic acid and L-lactic acid) of 100,000, beta-tricalcium phosphate (beta-TCP) with a mean particle diameter of about 3 micrometers was mixed to homogeneity 80weight % by the same method as Embodiment 1, and suspension was prepared. It is checked that this beta-TCP

is living body activity and absorptivity in the living body, and, as for a mechanism, it is known that it shows osteoconductivity by HA generation in the living body although u-HA differs.

[0058]By carrying out compression molding and carrying out solvent dipping treatment of nothing and this to a fiber set Plastic solid using this suspension, under heating of a fiber aggregate produced with a spray method like Embodiment 2, in continuation porosity, 75%, in apparent relative density, about 0.6 obtained a compound porous body of 4.2MPa, and compressive strength obtained it. A volume ratio of a beta-TCP grain of this compound porous body is about 65 volume %, and since volume of an inorganic powder grain is [u-HA] quite larger than a compound porous body of 70weight % (about 55 volume %) of Embodiments 1 and 2, living body activity is notably revealed by exposure of beta-TCP to the surface and a stoma inner surface of a porous body.

[0059]Since this compound porous body is changing to a form with which fiber at the time of a nonwoven fabric state fiber aggregate disappeared, and a beta-TCP grain was buried in a cell wall of bulk state, While it did not break out easily that collapse also when immersed in body fluid in the living body, and this powder is distributed around but good living body activity was shown in about three to five months, it was checked that decomposition absorption is carried out thoroughly. therefore, hard tissue (a bone, a cartilage) with this good compound porous body -- it becomes a scaffold of business.

[0060][Embodiment 4] D, L-lactic acid (mole ratio 1 of D/L), and glycolic acid (GA) were blended so that the mole ratio might be set to 8:2, and viscosity average molecular weight compounded the copolymer P of 130,000 (DLLA-GA) by a known method. By the same method as Embodiment 1, suspension which mixed octacalcium phosphate (OCP) to homogeneity 60weight % is prepared to this polymer, Apparent relative density obtained a compound porous body of 0.50 eventually by carrying out compression molding and carrying out solvent dipping treatment of nothing and this to a fiber set Plastic solid under heating of a fiber aggregate produced with a spray method like Embodiment 2. Three to four months afterward that most was absorbed, and this compound porous body was replaced by a bone, while decomposition absorption of a copolymer originated in GA, and good bone conduction (changeable to a new bone) was shown, since activity of OCP was high, and it was quick.

[0061][Embodiment 5] It blended so that the mole ratio might be set to 8:2 in D,L-lactide (lactide) and ****- dioxa non (p-DOX), and copolymerization was carried out by a known method, and viscosity average molecular weight obtained about 100,000 copolymer. Although a volatile good solvent with general-purpose polymer of p-DOX was not found, since it became meltable to chloroform, dichloromethane, etc. by the above-mentioned ratio, a compound

porous body made into the purpose by the same method as an embodiment mentioned above was able to be obtained. Since the above-mentioned copolymer shows description like [which is reversible from D of Embodiment 4, and the copolymer P of L-lactic acid and glycolic acid (DLLA-GA)] rubber, since a volume ratio of an inorganic powder grain is highly made with 70 volume % (85 weight %) when particle diameter of an inorganic powder grain is 3 micrometers, a vital reaction according [this compound porous body] to a decomposition product of a copolymer is avoided as much as possible -- a living body -- activity of an activity inorganic powder grain is revealed very effectively. In particular, from the characteristic of p-DOX, since hydrophilic nature is higher than PDLLA, it is thought that this compound porous body is effective in a scaffold of reproduction of a cartilage for proliferating a cell by Ex vivo (external petri dish), etc.

[0062]

[Effect of the Invention]So that clearly from the above explanation organic - inorganic matter compound porous body of this invention, Contain a lot of inorganic powder grains by the uniform dispersion state in organic polymer, and body fluid etc. permeate promptly through the large continuation stoma of the aperture formed in the inside, By inorganic powder grains, such as bioceramics exposed to the surface or the inner surface of a continuation stoma, the place which can perform combination with a body bone and a rebirth of a living body (bone) organization at an early stage is provided, and the effect of also having practical strength required for a medical-application way is done so. Therefore, it uses as the inclusion between the scaffold for body bone organization reconstruction, prosthetic dentistry material, a bone filler, the implant, and a body bone organization, the substitute of a cancellous bone, and a carrier for drug gradual release.

[Translation done.]

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TECHNICAL FIELD

[Field of the Invention]This invention about organic-inorganic matter compound porous body The scaffold especially for body bone anagenesis (Scaffold), It is related with organic-inorganic matter compound porous body suitable for the use of the inclusion between prosthetic dentistry material, a bone filler, the implant, and a body bone organization, the substitute of a cancellous bone, the carrier for drug gradual release of DDS (Drug Deliverly System), etc.

[Translation done.]

PRIOR ART

[Description of the Prior Art]As an inorganic porous body aiming at a medical-application way, temporary quenching or the porous ceramics produced by sintering (Calcined, Sintered) are known in Ceramics Sub-Division, for example. However, although these porous ceramics are hard for using it for uses, such as a scaffold for body bone organization reconstruction, and prosthetic dentistry material, since there is a fault that it is weak, it is always apprehensive about breakage by few postoperative shocks. It is also difficult to process it and to change the form of porous ceramics at the operation spot so that the form of the lacking part of a body bone organization may be suited.
[0003]On the other hand, the sponge etc. which were indicated by JP,63-64988,B are known as an organic porous body aiming at a medical-application way, for example. This sponge is sponge which has ordinarily a continuation stoma which is used as a prosthetic dentistry material at the time of the hemostasis at the time of an operation, or a suture of a living body's tissues (for example, organ etc.), and consists of polylactic acid of biodegradation absorptivity. This sponge dissolves polylactic acid in benzene or dioxane, and is manufactured by the method which freeze-dries the polymer solution and to which a solvent is made to sublimate.
[0004]However, the porous body manufactured by a freeze drying method like the above-mentioned sponge is difficult for sublimation to take a long time and to remove a solvent thoroughly, and the thickness is as thin as 1 mm or less (usually about hundreds of micrometers), and it is actually difficult to manufacture a not less than several millimeters thick porous body. Although various methods are examined besides the above-mentioned freeze drying method as other methods of building the porous body which has a continuation stoma, it is difficult for all to obtain a several millimeters thick porous body. Such a thin porous body is geometrically applied to the complicated and

comparatively large three dimensional space of for example, a body tissue damaged area, and there is difficulty in considering it as the material which aims at organization reconstruction of a three-dimensional damaged area, demonstrating the function as primary prosthetic dentistry material. Then, thickness is large and what can work on a free-shaped three-dimensional cube before an operation or after the operation is called for.

[0005]The powder of fusibility, such as NaCl etc. of the predetermined size which is water solubility, is mixed so much to polymer as another leading method of building a continuation porous body, After building the molded product of sheet shaped closing in, the melting which forms the continuous pores of the same path as this powder by being immersed in water (solvent) and eluting this powder is known, but since it is difficult to elute this powder thoroughly, it is limited to the continuation porous body of closing in. If the ratio of a water-soluble powder becomes high, it will be hard to become an open cell. And when using this porous body as an embedding material in the living body, there is a problem of troubling to the toxicity of this powder that remains.

[0006]the above-mentioned sponge -- like -- a living body -- the porous body which does not include inorganic powder grains, such as activity bioceramics, Direct unity with body bone organizations, such as a bone and a cartilage (direct bondingability to bone), Since conductivity (osteoconductivity), replaceability (bone replacement), etc. are scarce and the tissue which is not osteoblast invades and intervenes, It finishes as a remarkable long period of time is taken for a living body's osseous tissue to replace thoroughly and to reproduce it or it is not replaced.

[0007]Then, seeding of these people is carried out in osteoblast, and they become a scaffold of a three-dimensional cube, the lacking part of a big bone -- a pons -- it already applied for the porous body with large thickness which has a continuation stoma which becomes an inside which can be planted for me from the biodegradation absorption polymer which the bioceramics powder contained (Tokuganhei8-229280).

[0008]This porous body is based on the manufacturing method of the porous body called a solution sedimentation method. Namely, dissolve a biodegradation absorption polymer in a mixed solvent with the nonsolvent of a high boiling point from the solvent and its solvent, and. A bioceramics powder is distributed, suspension is prepared, a mixed solvent is aerated at low temperature from the boiling point of a solvent from this suspension, and it is based on the method of settling the biodegradation absorption polymer which includes a bioceramics powder.

[0009]The formation principle of the porous body by this solution sedimentation method is as follows. If a mixed solvent is aerated at low temperature from the

boiling point of a solvent from the above-mentioned suspension, the low solvent of the boiling point will exhale preferentially and the ratio of the high nonsolvent of the boiling point will rise gradually, and when a ratio with a solvent and nonsolvent is reached, it becomes impossible that is, for a solvent to dissolve polymer. Therefore, the bioceramics powder which polymer started a deposit and precipitate and has started sedimentation at the beginning is included, It is fixed the polymer which deposited and precipitated contracting and solidifying with the nonsolvent of a high ratio, and containing a bioceramics powder, and the cellular structure in the state where the mixed solvent was included by the connected thin cell wall of polymer is formed. And fine pores are built, while the remaining solvents destroy some cell walls, it disappears and exhalation and the high nonsolvent of the boiling point also exhale gradually through these fine pores, and it exhales and disappears thoroughly finally. As a result, the bioceramics powder content porous body with which the remains of a reservoir of the mixed solvent wrapped in the cell wall of polymer were connected as a continuation stoma is formed.

[Translation done.]

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EFFECT OF THE INVENTION

[Effect of the Invention]So that clearly from the above explanation organic - inorganic matter compound porous body of this invention, Contain a lot of inorganic powder grains by the uniform dispersion state in organic polymer, and body fluid etc. permeate promptly through the large continuation stoma of the aperture formed in the inside, By inorganic powder grains, such as bioceramics exposed to the surface or the inner surface of a continuation stoma, the place which can perform combination with a body bone and a rebirth of a living body (bone) organization at an early stage is provided, and the effect of also having practical strength required for a medical-application way is done so. Therefore, it uses as the inclusion between the scaffold for body bone organization reconstruction, prosthetic dentistry material, a bone filler, the implant, and a body bone organization, the substitute of a cancellous bone, and a carrier for drug gradual release.

[Translation done.]

TECHNICAL PROBLEM

[Problem to be solved by the invention]The above-mentioned solution sedimentation method is the epoch-making method of forming a porous body with large thickness of high expansion ratio from low foaming magnification, and can obtain the three-dimensional porous body of the block like shape which has a thickness of several millimeters thru/or tens of mm. So, in the scaffold of the osteoanagenesis of cubic shape (three-dimensional spacial configuration), it is very useful.

[0011]However, with the suspension which contained the bioceramics powder in large quantities, the fault of this method. When the bioceramics powder which belongs to comparatively big particle size distribution among mean particle diameter starts sedimentation at the beginning which begins solvent vaporization and polymer starts a deposit and precipitate, Since the remarkable bioceramics powder has already sedimented with a concentration gradient towards a pars basilaris ossis occipitalis, content of the porous body obtained increases as the content of a bioceramics powder is not selectively uniform and approaches the bottom side from the upper surface side of a porous body. Thus, content cannot use the uneven porous body with a concentration gradient for uses, such as a scaffold for osseous tissue reconstruction, prosthetic dentistry material, or a bone filler, easily effectively. This problem is thoroughly unsolvable although it is possible to improve to some extent by controlling the sedimentation velocity of a bioceramics powder, etc. It is difficult especially to consider it as the porous body with the homogeneous and equal concentration which contains a thing bioceramics powder 30weight % or more for three-dimensional bone reconstruction.

[0012]A porous body with little content of a bioceramics powder manufactured by an above-mentioned method, Since most bioceramics powders are included by cell wall of polymer and it is hard to expose it to an inner surface of a

continuation stoma, When it embeds in the living body, a conduction operation of a body bone organization by a bioceramics powder is hard to be demonstrated from the time of embedding, and there is a problem that living body activity is revealed with a bioceramics powder exposed [decomposition of polymer which forms a skin of a continuation stoma inner surface].

[0013]Though a porous body manufactured by an above-mentioned method chooses a super-thin grain, if it needs to carry out content of a bioceramics powder to to about at most 30 weight % and a large quantity is made to contain it from this, Since a bioceramics powder sediments much more easily, there is a limit that the bottom side of a porous body obtained becomes very weak including a lot of bioceramics powders.

[0014]Although a porous body manufactured by an above-mentioned method usually has a rate (porosity) as large as not less than 80% that a continuation stoma occupies, Generally, since only several micrometers thru/or tens of micrometers, and a comparatively small continuation stoma are obtained, an aperture cannot say that a form of an aperture ideal for invasion and growth of osteoblast inside a porous body and a hole is formed.

[0015]An object of this invention is to provide the manufacturing method to organic-inorganic matter compound porous body which can solve these problems.

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MEANS

[Means for solving problem]An inorganic powder grain distributes uniformly substantially in organic polymer, organic - inorganic matter compound porous body concerning this invention is a porous body which has a continuation stoma inside, and a part of inorganic powder grain exposes it to the surface and stoma inner surface. And a continuation stoma is adjusted by about 100-400 micrometers in the suitable aperture for osteoblast to increase and invade and be stable, and the inorganic powder grain is contained so much with 60 to 90 weight %. The thickness of a porous body is as large as 1-50 mm, and has three-dimensional cubic shape.
[0017]Such an organic-inorganic matter compound porous body builds a nonwoven fabric state fiber aggregate with the manufacturing method of this invention, i.e., the suspension which dissolved organic polymer in the volatile solvent, were made to distribute an inorganic powder grain, and was prepared, It can manufacture by the method of carrying out pressing under heating of this, and removing this solvent after ranking second and immersing a fiber set Plastic solid in a volatile solvent, a porous fiber set Plastic solid, nothing, and. As a means which builds a nonwoven fabric state fiber aggregate with suspension, When the means which carries out a spray is adopted preferably and a fiber set Plastic solid is immersed in a volatile solvent, fibrosing suspension, what external force which holds the form of a fiber set Plastic solid is applied for is desirable, and, thereby, a porous body with a mechanical strength is obtained.
[0018]As mentioned above, if the means which carries out a spray is adopted fibrosing the adjusted suspension as a means which builds a fiber aggregate, Fiber of organic polymer included the inorganic powder grain becomes entangled mutually, and ****s at a mutual point of contact, fiber carries out set solidification by the vaporization of a volatile solvent, and a nonwoven fabric state fiber aggregate with arbitrary heavy-gage form is formed. This fiber

aggregate has the continuous space whose interval between fiber which carried out welding solidification is about hundreds of micrometers although fiber interspace spare time is not a cell-like hole (round cell space), and an inorganic powder grain is included by fiber, covers the whole fiber aggregate, and is distributed uniformly. Pressing is carried out under heating of this fiber aggregate, a porous fiber set Plastic solid is built, and if immersed in a volatile solvent, holding that form applying external force, fiber will contract and unite. And a fibrous form disappears substantially and fiber interspace spare time becomes the porosity matrix which carried out the shape change to the continuation stoma object with the cellular structure which has a radius of circle. And that part exposes to a stoma inner surface the inorganic powder grain contained so much with this transformation, and. It exposes by ********** to such an extent that an inorganic powder grain does not drop out easily on the surface, and organic-inorganic matter compound porous body made into the purpose, i.e., an inorganic powder grain, distributes uniformly substantially with high content, and organic - inorganic matter compound porous body which the part exposed to the surface or the inner surface of a continuation stoma is obtained. Of course, when a skin is formed in the surface of conditions, an inorganic powder grain may be exposed by carrying out sanding. This compound porous body by adjusting the external pressure for holding that form, when a fiber set Plastic solid is immersed in a volatile solvent, The average pore size of a continuation stoma is controllable to convenient about 100-400 micrometers for invasion and stabilization of osteoblast, and it is desirable to make porosity into a stoma form with about 50 to 90% of desirable conditions.

[0019]It is possible to make the stoma inside of the body contain uniformly 60 to 90weight % (equivalent to 41-81 volume %, when mean particle diameter is 3 micrometers) of an inorganic powder grain in the manufacturing method of this invention within limits which can fibrose. Since this fiber ****s before an inorganic powder grain sediments, even if it makes it contain so much, rather than the porous body obtained with the solution sedimentation method mentioned above, the inorganic powder grain is distributing uniformly and content can obtain a far high compound porous body eventually. However, if it is high content too much, it will become difficult for the amount of polymer as a binder to decrease, and for a porous body to become weak, and to maintain form.

[0020]Even if the solvent characteristic has balanced this manufacturing method, is already used as organic polymer, safety is confirmed, this organic-inorganic matter compound porous body aiming at medical-application ways, such as a scaffold for body bone anagenesis, has comparatively quick

decomposition and it becomes a porous body, polymer which is not weak is chosen. Namely, the block copolymer of Polly D in whom it was amorphous or a crystal and non-** were intermingled, L-lactic acid, L-lactic acid, and D and L lactic acid, Biodegradation absorption polymers, such as copolymers of lactic acid, the copolymer of glycolic acid and lactic acid, the copolymer of p-dioxa non and lactic acid, the copolymer of a caprolactone and lactic acid, and ethylene glycol or these mixtures, are used. In consideration of the period of that the viscosity average molecular weight tends to form a nonwoven fabric state fiber aggregate and decomposition absorption in the living body, the thing of 50,000-1 million is used preferably.

[0021]The block copolymer of Polly D who originates in a monomer ratio and shows amorphism nature especially, L-lactic acid, L-lactic acid, and D and L lactic acid, Biodegradation total absorption nature polymer, such as a copolymer of lactic acid and glycolic acid, lactic acid, a copolymer of p-dioxa non, If it is suitable and these polymer is used under heating of this, in view of the solvent characteristic when processing the fiber set Plastic solid which carried out pressing by a volatile solvent when forming a nonwoven fabric state fiber aggregate and, Even if it includes a lot of inorganic powder grains, it has about the same compressive strength (compressive strength of about 1-5 MPa) as a cancellous bone easily, Organic - inorganic matter compound porous body by which can carry out heat modification at low temperature (about 70 **) comparatively unlike the porous body of a ceramic simple substance, hydrolyzes promptly in the living body, and total absorption is carried out in six to 12 months can be obtained. The compound porous body which has such the characteristic is very preferred as a biomechanical material with which the lacking part of a body bone is filled up. Although it is a complex therefore, it has also left the advantage peculiar to thermoplastic polymer which can prepare a form so that heat modification may be carried out during an operation unlike the material of only Ceramics Sub-Division and it may agree in a lacking part.

[0022]Since it hydrolyzes and the molecular weight of biodegradation total absorption nature polymer affects time until total absorption is carried out, and the propriety of fibrosis, the polymer which has the viscosity average molecular weight of 50,000-1 million as mentioned above is used. Although the time when the polymer which has viscosity average molecular weight smaller than 50,000 is hydrolyzed by the low molecule of oligomer thru/or a monomeric unit is short, it is difficult to carry out a spray and to form a bicomponent fiber aggregate, fibrosing, since stringiness runs short. Since it takes a long period of time to carry out complete hydrolysis of it, the polymer which has larger viscosity average molecular weight than 1 million is unsuitable as polymer of a compound porous body, when aiming at early substitution with a body tissue. Although it

changes with polymer, that desirable viscosity average molecular weight is the profiles 100,000-300,000, and if the polymer which has a molecular weight of this range is used, it can obtain the compound porous body of this invention which formation of a fiber aggregate becomes easy and has moderate hydrolysis completion time.

[0023]In organic-inorganic matter compound porous body aiming at the above-mentioned medical-application way, as an inorganic powder grain, there is living body activity and the bioceramics powder which has good osseous conduction capacity (it is supposed that bone induction potency is sometimes shown) and good biocompatibility is used. As such a bioceramics powder, for example, a surface living body -- activity calcination, temporary calcination hydroxyapatite, and apatite WORASUTO night crystallized glass. Non-temporary quenching of living body activity and total absorption nature in the living body, uncalcinated hydroxyapatite, Powders, such as JIKARUSHIUMU phosphate, tricalcium phosphate, tetracalcium phosphate, octacalcium phosphate, calcite, cera liveliness, a JIOPU site, and natural coral, are mentioned. The thing which made an alkaline inorganic compound, basic organic matter, etc. adhere to the surface of these powders is also usable. According to the Reason it is ideal that succeed in total replacement arthroplasty with one's body tissue, and anagenesis is performed. The bioceramics granular material of the total absorption nature in the living body which total absorption is carried out and is thoroughly replaced by an osseous tissue also in these in the living body is preferred, Activity is the largest, they are excellent in osseous conduction capacity, are excellent in biocompatibility, their harmfulness is low, and since especially non-temporary quenching, uncalcinated hydroxyapatite, tricalcium phosphate, and octacalcium phosphate are absorbed by the living body for a short period of time, they are the optimal.

[0024]If it is preferred that particle diameter uses a thing of 10 micrometers or less as for the above-mentioned bioceramics powder and the bioceramics powder of larger particle diameter than this is used, When carrying out a spray, fibrosing the suspension which mixed this powder, fiber is cut short, and even if it becomes difficult to form a fiber aggregate and it is able to form a fiber aggregate, there will be a possibility of a bioceramics powder sedimenting somewhat by the time fiber solidifies, and distributing unevenly. Since full absorption takes a long time and a tissue reaction in the meantime is sometimes revealed even if it is total absorption nature, the thing of the size over 20-30 micrometers is not preferred.

[0025]If the still more desirable particle diameter of a bioceramics powder is 0.2-5 micrometers and such a bioceramics powder is used, Even when fibrosing thinly the suspension which mixed this powder to high concentration with about

1-3 micrometers and forming a fiber aggregate in it like this invention, Fiber is hard to be cut, and when it is high concentration like this invention, after this powder comes to be included by fiber in the state where it exposed from fiber and carries out dipping treatment of the fiber aggregate by a volatile solvent, this powder serves as a compound porous body exposed from the surface or the inner surface of the continuation stoma.

[0026]The carrier or bone filler for a scaffold [in / in the content of a bioceramics powder / tissue engineering], or DDS, In the case of organic-inorganic matter compound porous body aiming at medical-application ways, such as a substitute of an anomaly-like cancellous bone (Allograft: piece of congener different **), it is preferred to consider it as 60 to 90 weight %, considering the living body activity effect of bioceramics. When the aggregate of the fiber which included the inorganic powder grain like this invention is formed, the fiber set Plastic solid which carried out pressing of this under heating is immersed in a volatile solvent and it obtains a compound porous body, Since a lot of inorganic powder grains can be made to contain within limits which can fibrose, the content of a bioceramics powder can be raised as mentioned above with 60 to 90 weight % (the volume ratio at the time of the mean particle diameter of 3 micrometers is equivalent to the high ratio of 41 to 81%). Since it will go out short and will not become satisfactory fiber, when fibrosing if the content of a bioceramics powder exceeds 90 weight %, if formation of a fiber aggregate becomes difficult and is less than 60 weight % on the other hand, Bioceramics powders run short, and since what is exposed to the surface is little, the living body activity which originates in a bioceramics granular material from the first stage embedded to the living body is hard to be revealed.

[0027]Although the porous ceramics produced by sintering Ceramics Sub-Division, such as hydroxyapatite, are hard, since it is weak, since thin material breaks easily with external force or is missing, it is dissatisfied as implant. On the other hand, the compound porous body which made the biodegradation absorption polymer which is amorphism nature especially contain a bioceramics granular material, Even when the content of a bioceramics granular material is as high as 60 to 90 weight %, by the joint (binding) effect of the polymer. The compressive strength of the cancellous bone average holding flexibility which is not weak, and since it specifically has about [1MPa-5MPa] compressive strength, it is suitably used as substitution (for of-the-same-kind bone grafting: substitution of Allograft bone) of a cancellous bone, a bone filler, prosthetic dentistry material and the scaffold for reproduction, or a carrier of DDS.

[0028]moreover -- as another leading use -- a body bone (a bone, a cartilage) -- the inclusion between the artificial implant of business is mentioned. For example, since it is inescapable that a crevice arises among living bodies when

embedding the artifact which has the high concentration built with polylactic acid system polymer of entering [which is the osteosynthesis material of living body activity and living body absorptivity] bioceramics powder, If it intervenes and this compound porous body is directly contacted to an osseous tissue in the meantime, osteoconductivity will be revealed notably. Although this works effectively by various parts of a body bone, bone derivation (concomitant use with cytokine) and bone conduction can be brought about into the hollow-ized intense bone of osteoporosis (osteoporosis) by embedding the sternum lock-pin which made the Ko Honda object penetrate in the case of median sternotomy for example to the Masanaka bone. Or it can use as an underlay of this kind of plate, and adhesion with a bone can also be aimed at. The use as inclusion of a living body and an artifact has aiming at [much] direct combination to an artificial intervertebral disk and a centrum end plate (endplate) etc.

[0029]Although porosity (total porosity) is not less than 50% and this organic - inorganic matter compound porous body is technically possible to about 90%, If the both sides of the physical intensity of this compound porous body, invasion of osteoblast, and stabilization are taken into consideration, 60 to 80% of a profile is good, and considering the efficiency of invasion of the osteoblast to the central part of a compound porous body, the thing of the whole stoma for which a continuation stoma occupies 70 to 90% above all 50 to 90% is preferred.

[0030]As for the continuation stoma of this organic-inorganic matter compound porous body, that aperture is adjusted to 100-400 micrometers of profiles. It turns out that an effect fades as it has already succeeded in the aperture of porous ceramics, invasion of osteoblast, and research of stabilization many times, and 300-400 micrometers in their aperture is the most effective for mineralization and separates them from it, considering the result. So, although the aperture of the compound porous body of this invention is adjusted by 100-400 micrometers of profiles as mentioned above, a center of a distribution may be 200-400 micrometers including the thing of the aperture of the range of 50-500 micrometers.

[0031]Incidentally, when porosity (total porosity) is higher than 90%, since the intensity of a compound porous body falls, a possibility of destroying easily during [in the living body] embedding is large [the aperture of a continuation stoma is larger than 400 micrometers, and]. On the other hand, when an aperture is smaller than 100 micrometers and porosity is lower than 50%, the intensity of a compound porous body improves, but invasion of osteoblast is difficult, it hydrolyzes and time until it carries out full absorption becomes long. However, the small compound porous body of low porosity of such an aperture is available by a case as a material which desires to maintain sustained-release

[of comparatively long time to do simultaneously with decomposition of polymer as a carrier of DDS]. The more desirable aperture of a continuation stoma is 150-350 micrometers, and more desirable porosity (total porosity) is 70 to 80%. The ratio of the continuation stoma to the aperture of a continuation stoma, and the whole stoma, As mentioned above, it is controllable by regulation of a compression ratio when carrying out pressing of the fiber aggregate and making with a fiber set Plastic solid, and regulation of the external pressure for form maintenance in case the form is held and a fiber set Plastic solid is immersed in a volatile solvent.

[0032]The above organic - inorganic matter compound porous bodies can be used, for example as implant of various form, being able to embed to the deficit part of a body bone. Since it can embed that there is no crevice in defective parts by making it change so that a compound porous body may be heated at about 70 ** using the thermoplasticity of organic polymer and it may agree in the form of defective parts in that case, it becomes possible to do embedding work simply and correctly. A scalpel can also use from arbitrary form during an operation for the hardness of the toughness which organic polymer has, and a ceramic powder, cutting without form collapse.

[0033]A compound porous body For example, since body fluid will permeate the inside of a compound porous body promptly through the inside of a continuation stoma from the surface of a compound porous body if it embeds in a living body's osseous tissue as mentioned above, Since hydrolysis of a biodegradation absorption polymer advances almost simultaneous from the both sides the surface of a compound porous body, and inside a continuation stoma, The whole porous body is covered and decomposition advances uniformly (however, it gets wet, and the bioceramics powder with living body liquid which contained the characteristic so much and was exposed to the surface gets wet, and with the characteristic.). It is improving more remarkably than the case of only polymer, or polymer gets wet, and oxidation treatments, such as corona discharge, plasma treatment, and hydrogen-peroxide-solution processing, may be performed to a porous body in order to make more effective invasion of the cell which should also improve the characteristic and should be increased, and growth. And the compound porous body embedded to the part which osteocyte exists or contacts osteocyte, With the osseous conduction capacity of the bioceramics powder exposed to the surface, conduction formation is carried out promptly, and an osseous tissue becomes the bony trabecula (trabecularbone) and grows up to be a layer part of a compound porous body, Since a compound porous body combines with the deficit part of a body bone within a short period of time, and an osseous tissue invades also into the inside of a compound porous body, osteoblast conducts and it grows up with the osseous conduction

capacity of the bioceramics powder exposed to a stoma inner surface, it couples directly with a circumference bone. This phenomenon becomes remarkable with advance of decomposition of a biodegradation absorption polymer, and is gradually replaced by a circumference bone. And decomposition absorption of the polymer is carried out thoroughly eventually, and when a bioceramics powder is absorptivity in the living body, a bioceramics powder is also absorbed thoroughly, and it is thoroughly replaced by the grown-up osseous tissue, and reproduction of a bone lacking part is completed.
[0034]Speed by which decomposition absorption is carried out as a scaffold for living body reconstruction of which the above total replacement arthroplasties are required is balanced, By making various growth factors, such as cytokine which are beforehand filled up in a stoma, or were dissolved beforehand and made to support in polymer, drugs for various therapies, an antimicrobial agent, etc. release gradually, living body reproduction and sick recovery can be promoted, or it can be made effective. It is clear that the above-mentioned compound porous body naturally becomes a filler and prosthetic dentistry material of a deficit organization with combination with a bone (Allograft bone) independent or of the same kind as point ** was carried out.
[0035]Although the above-mentioned organic - inorganic matter compound porous body is total replacement arthroplasty or the things in part aiming at a medical-application way, such as inclusion between a scaffold for replaced type body tissue reproduction, a carrier of drugs, prosthetic dentistry material, a bone filler, implant, and a body tissue, and a substitute of a cancellous bone, In the case of organic-inorganic matter compound porous body aiming at other uses, according to a use, selection use of polymethylmethacrylate, polyvinyl acetate, polyvinyl chloride, polyurethane, polyalkylene oxide, and various kinds of general-purpose resin meltable to other volatile solvents is suitably carried out as organic polymer. And as for an inorganic powder grain, according to a use, selection use of various kinds of industrial use fillers, a functional filler, a ceramic powder, carbon powder, the carbon nanotube, etc. is carried out suitably.
[0036]Next, a manufacturing method of this invention is explained.
[0037]According to the manufacturing method of this invention, first, the above-mentioned organic polymer is dissolved in a volatile solvent, and the above-mentioned inorganic powder grain is distributed uniformly, and suspension is prepared. Solvents, such as low-boiling-point dichloromethane which vaporizes easily at a temperature a little higher than ordinary temperature as a volatile solvent, a dichloroethane, a methylene chloride, and chloroform, are used. To these solvents, nonsolvent in which the boiling point is higher than these solvents. for example, either of alcohol, such as methanol in a

range whose boiling point is 60-110 **, ethanol, 1-propanol, 2-propanol, 2-butanol, ter-butanol, and a ter-pentanol, -- a volatile mixed solvent which was independent or mixed two or more sorts is also used.
[0038]Subsequently, suspension is attached to a spray machine to close, and a spray is carried out, fibrosing suspension from a nozzle of a spray machine to an injection body by high-pressure-jet gas [inertness / nitrogen gas]. Thus, if a spray is carried out, it will solidify, while suspension fibroses, it becomes entangled mutually and fiber ****s at a mutual point of contact, a volatile solvent vaporizing, and a nonwoven fabric state fiber aggregate will be formed. What is necessary is to wait for a solvent to vaporize and dry, to repeat again operation which carries out a spray and is made heavy-gage on it, and just to make it become thick [predetermined], after forming this fiber aggregate with a spray, in order to obtain a 5-50 sometimes required as a biomechanical material of a medical-application way mm heavy-gage compound porous body.
[0039]Gauze and the board which consist of other good polyethylene and olefin system resin of detachability, a fluoro-resin, silicon system resin, etc. as an injection body are used. Since a volatile solvent will vaporize through meshes of a net after suspension's fibrosing with a spray and hitting gauze if the injection body in which aeration like gauze is free is used especially, Fiber of the surface by the side of gauze unites, a skin is not produced, and there is an advantage which can form the fiber aggregate which the impregnation of a solvent tends to carry out. The gauze in which the thing of 50-300 meshes is preferred, and has larger meshes of a net than 50 meshes as gauze, Since a volatile solvent does not vaporize easily smoothly, fiber by the side of gauze unites the gauze which exfoliating from gauze comes to be hard of the formed fiber aggregate, and has meshes of a net smaller than 300 meshes since fiber turns to the back side through meshes of a net, and a skin becomes is easy to be formed. An injection body may use flat gauze or not only a board but convex-curved, and/or three-dimensional gauze and board which carried out the concave bend. When such a three-dimensional injection body is used, there is an advantage which can form the heavy-gage fiber aggregate as the three-dimensional form.
[0040]The fiber aggregate formed by carrying out a spray while fibrosing suspension as mentioned above has a size of fiber interspace spare time as large as hundreds of micrometers, and the percentage (voidage) that fiber interspace spare time occupies is about 60 to 90%. And without an inorganic powder grain's being included by fiber and sedimenting, the whole fiber aggregate is covered and it is distributing uniformly.
[0041]As for the fiber length of this fiber aggregate, it is preferred that it is about 3-100 mm, and, as for a fiber diameter, it is preferred that it is about 0.5-50 micrometers. Fiber unites easily the fiber aggregate which has fiber length of

this level and fiber diameter by the impregnation of a next solvent, and it turns into a compound porous body in which fiber disappeared substantially.
[0042]Fiber length is in the tendency which becomes long, so that a molecular weight becomes large mainly depending on the molecular weight of organic polymer, the polymer concentration of suspension, content, particle diameter of an inorganic powder grain, etc., polymer concentration becomes high, the content of an inorganic powder grain decreases and the particle diameter of an inorganic powder grain becomes small. On the other hand, a fiber diameter is in the tendency which becomes thick, so that polymer concentration becomes high mainly depending on the polymer concentration of suspension, the content of an inorganic powder grain, the size of the nozzle of a spray machine, etc., the content of an inorganic powder grain increases and a nozzle becomes large. A fiber diameter changes also with the pressures of injection gas. Therefore, it is required to prepare the content of the molecular weight of polymer, polymer concentration, and an inorganic powder grain, particle diameter and the size of a nozzle, gas pressure, etc. so that it may become the above-mentioned fiber length and a fiber diameter.
[0043]The above-mentioned fiber aggregate ranks second, and under heating, pressing of it is carried out and it is used as a porous fiber set Plastic solid. It is desirable to build the preforming thing which has the void which hardened the fiber aggregate under heating and application of pressure first, and continued in that case, to carry out pressing of the preforming thing under high voltage further more, and to consider it as the fiber set Plastic solid of porosity with the intensity to which the intercommunicating porosity hole was adjusted. Thus, if pressing is carried out and a porous fiber set Plastic solid is built, the aperture and porosity of a continuation stoma of a compound porous body which are obtained eventually can be adjusted, and the intensity of a compound porous body can also be raised. The grade which a fiber aggregate softens for a while is enough as heating at the time of pressing, and what is necessary is just to perform application of pressure by a pressure compressible so that the aperture of a continuation stoma serves as 100-400 micrometers of profiles so that the porosity of the compound porous body obtained eventually may be 50 to 90%.
[0044]Subsequently, after immersing this fiber set Plastic solid in a volatile solvent and making this solvent permeate the inside of a Plastic solid, this solvent made to permeate is removed. When a fiber set Plastic solid is immersed in a volatile solvent, it is preferred to be immersed holding form, where it filled up with the fiber set Plastic solid the predetermined mold which has much fine pores and a pressure is applied to a fiber set Plastic solid from the outside. A solvent is poured on the upper surface of a fiber set Plastic solid,

and it may be made to make it permeate. As a method of removing a solvent, the method of carrying out vacuum suction of the solvent inside a fiber set Plastic solid, etc. are adopted.
[0045]The dichloromethane, dichloroethane, methylene chloride which were mentioned above as a volatile solvent, either of alcohol, such as methanol of the above-mentioned [solvents / solvents, such as chloroform and / these], ethanol, 1-propanol, 2-propanol, 2-butanol, ter-butanol, and a ter-pentanol, -- what was independent or mixed two or more sorts is used preferably.
[0046]Since fiber will melt into a solvent from the surface if a fiber set Plastic solid is immersed in a volatile solvent as mentioned above and a solvent is made to permeate the inside of a Plastic solid, Fiber unites, fiber disappears substantially, and a cellular wall is formed where the continuation stoma in which fiber interspace spare time had a radius of circle which has an aperture which is about 100-400 micrometers is left. And it exposes to a stoma inner surface (cellular wall surface), without sedimenting with fusion of fiber, and a part of inorganic powder grain included in fiber is exposed also to the porous body surface. However, what is necessary is to remove by carrying out sanding of this, and just to take the measures to which the inorganic powder grain which exists in a surface is exposed, when a skin is formed in the surface. By the above, an aperture has 100-400 micrometers and a large continuation stoma, and a lot of inorganic powder grains distribute uniformly, and organic - inorganic matter compound porous body which the inorganic powder grain exposed to the surface and a stoma inner surface and which is made into the purpose is obtained. In that case, if dipping treatment to the volatile solvent of a fiber set Plastic solid is performed under 50-60 ** heating, only by neglecting a fiber set Plastic solid for 5 to 10 minutes, fiber can fully unite and the compound porous body made into the purpose can be obtained efficiently.
[0047]Organic-inorganic matter compound porous body obtained by the above manufacturing method, As mentioned already, the scaffold for body bone organization reconstruction, prosthetic dentistry material, a bone filler, The inclusion between the implant and a body bone organization, the substitute of a bulk-shaped cancellous bone, It is effectively used as a carrier for drug gradual release, etc., and follows, Each of inclusion between the scaffold for body bone organization reconstruction, the prosthetic dentistry material, the bone filler, implant, and body bone organization which consist of this organic - inorganic matter compound porous body, substitutes of a bulk-shaped cancellous bone, and carriers for drug gradual release is contained in this invention.
[0048]
[Mode for carrying out the invention]Next, the concrete embodiment of this invention is described.

[0049][Embodiment 1] The polymer solution (100 ml of concentration-DLLA4g / dichloromethane) in which viscosity average molecular weight dissolved Polly D of 200,000, and L-lactic acid (PDLLA) (mole ratios 50/50 of D-lactic acid and L-lactic acid) in dichloromethane, By homogenizing uniformly the mixture liquid which mixed with ethanol the hydroxyapatite powder (u-HA) which is not calcinated [with a mean particle diameter of 3 micrometers], the suspension which mixed u-HA so that 230 weight sections might become comparatively to PDLLA100 weight section was prepared.
[0050]Use a HP-E airbrush (made by Anest Iwata) as a spray machine, attach the above-mentioned suspension to this to close, and with the nitrogen gas of 1.6 kg/cm^2. The spray was carried out to the gauze made from polyethylene (150 meshes) left about 120 cm, the fiber aggregate was formed, and the fiber aggregate was exfoliated from gauze. The fiber diameter of this fiber aggregate was about 1.0 micrometer, and, as for fiber length, about 10-20 mm and apparent relative density were 0.2.
[0051]The disc-like fiber set Plastic solid (30 mm in diameter and 5 mm in thickness) was acquired by cutting this fiber aggregate in a suitable size, filling up a cylinder female die 30 mm in diameter, and 30 mm in depth, and compressing with a male so that the apparent relative density of a fiber aggregate is set to 0.5.
[0052]Subsequently, after immersing the above-mentioned fiber set Plastic solid in the solvent which consists of dichloromethane which mixed ethanol, making this solvent permeate the inside of a Plastic solid and neglecting it at 60 ** for 10 minutes, vacuum suction removes the solvent inside a Plastic solid, Organic-inorganic matter compound porous body of 30 mm in diameter, 5 mm in thickness, and 70 weight % of content of u-HA was obtained.
[0053]When the partial cutting side of this compound porous body was observed with the electron microscope, fiber united and disappeared, the continuation stoma which has about 100-400 micrometers in a large aperture was formed, u-HA distributed uniformly, and u-HA was exposed to a stoma inner surface and the surface. The rate (continuation porosity) which occupies the apparent relative density of this compound porous body to the whole stoma of 0.5 and a continuation stoma was 75%, and compressive strength was 1.1MPa.
[0054][Embodiment 2] After building the disc-like fiber set Plastic solid (30 mm in diameter, and 5 mm in thickness) as a preforming thing and heating this at 80 ** in gear oven like Embodiment 1, it put into the chamber which has a diameter reduction part from which the size of a diameter differs, and pressed fit in the cylinder whose lower diameter is 10.6 mm. Thus, the compressive strength of the fiber set Plastic solid of the shape of a pillar rod by which pressing was carried out under heating was about 2.5 MPa(s).

[0055]Subsequently, pressing to such an extent that the syringe of the equal diameter which the hole opened around is filled up with the fiber set Plastic solid of the shape of this pillar rod, a pressure is applied from that upper surface and undersurface and the height of a pillar rod-like fiber set Plastic solid does not change. After being immersed in the solvent (60 **) which consists of dichloromethane which mixed 15weight % of methanol for 10 minutes, this solvent was removed and the compound porous body was obtained.
[0056]The electron microscope photograph of the surface which carried out sanding to the partial cutting side of this compound porous body takes the form of the porosity in which fiber disappeared, the aperture comprises an about 150-300-micrometer mixing hole, and the u-HA grain was exposed from the porous body surface or a stoma inner surface. The apparent relative density of this compound porous body was about 0.55, continuation porosity rose to 70% and compressive strength was rising to about 3.5 MPa(s). It is thought that full absorption of this compound porous body is carried out in about six months although it is dependent on an embedding part or size, considering the viscosity average molecular weight of PDLLA, the ratio of the quantity to occupy, and the biodegradation absorption feature in in vivo of u-HA with a mean particle diameter of 3 micrometers.
[0057][Embodiment 3] Viscosity average molecular weight compounded PDLLA (mole ratios 30/70 of D-lactic acid and L-lactic acid) of 100,000, beta-tricalcium phosphate (beta-TCP) with a mean particle diameter of about 3 micrometers was mixed to homogeneity 80weight % by the same method as Embodiment 1, and suspension was prepared. It is checked that this beta-TCP is living body activity and absorptivity in the living body, and, as for the mechanism, it is known that it shows the osteoconductivity by HA generation in the living body although u-HA differs.
[0058]By carrying out compression molding and carrying out solvent dipping treatment of nothing and this to a fiber set Plastic solid using this suspension, under heating of the fiber aggregate produced with the spray method like Embodiment 2, in continuation porosity, 75%, in apparent relative density, about 0.6 obtained the compound porous body of 4.2MPa, and compressive strength obtained it. The volume ratio of the beta-TCP grain of this compound porous body is about 65 volume %, and since the volume of an inorganic powder grain is [u-HA] quite larger than the compound porous body of 70weight % (about 55 volume %) of Embodiments 1 and 2, living body activity is notably revealed by exposure of beta-TCP to the surface and the stoma inner surface of a porous body.
[0059]Since this compound porous body is changing to the form with which

fiber at the time of a nonwoven fabric state fiber aggregate disappeared, and the beta-TCP grain was buried in the cell wall of bulk state, While it did not break out easily that collapse also when immersed in body fluid in the living body, and this powder is distributed around but good living body activity was shown in about three to five months, it was checked that decomposition absorption is carried out thoroughly. therefore, the hard tissue (a bone, a cartilage) with this good compound porous body -- it becomes a scaffold of business.

[0060][Embodiment 4] D, L-lactic acid (mole ratio 1 of D/L), and glycolic acid (GA) were blended so that the mole ratio might be set to 8:2, and viscosity average molecular weight compounded the copolymer P of 130,000 (DLLA-GA) by the known method. By the same method as Embodiment 1, the suspension which mixed octacalcium phosphate (OCP) to homogeneity 60weight % is prepared to this polymer, Apparent relative density obtained the compound porous body of 0.50 eventually by carrying out compression molding and carrying out solvent dipping treatment of nothing and this to a fiber set Plastic solid under heating of the fiber aggregate produced with the spray method like Embodiment 2. Three to four months afterward that most was absorbed, and this compound porous body was replaced by the bone, while decomposition absorption of the copolymer originated in GA, and good bone conduction (changeable to a new bone) was shown, since the activity of OCP was high, and it was quick.

[0061][Embodiment 5] It blended so that the mole ratio might be set to 8:2 in D,L-lactide (lactide) and ****- dioxa non (p-DOX), and copolymerization was carried out by the known method, and viscosity average molecular weight obtained about 100,000 copolymer. Although the volatile good solvent with general-purpose polymer of p-DOX was not found, since it became meltable to chloroform, dichloromethane, etc. by the above-mentioned ratio, the compound porous body made into the purpose by the same method as the embodiment mentioned above was able to be obtained. Since the above-mentioned copolymer shows the description like [which is reversible from D of Embodiment 4, and the copolymer P of L-lactic acid and glycolic acid (DLLA-GA)] rubber, since the volume ratio of an inorganic powder grain is highly made with 70 volume % (85 weight %) when the particle diameter of an inorganic powder grain is 3 micrometers, the vital reaction according [this compound porous body] to the decomposition product of a copolymer is avoided as much as possible -- a living body -- the activity of an activity inorganic powder grain is revealed very effectively. In particular, from the characteristic of p-DOX, since hydrophilic nature is higher than PDLLA, it is thought that this compound porous body is effective in the scaffold of reproduction of the cartilage for

proliferating a cell by Ex vivo (external petri dish), etc.

[Translation done.]